

Original Contribution

New-Onset Asthma and Combat Deployment: Findings From the Millennium Cohort Study

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Recent reports suggest US military service members who deployed in support of the recent conflicts in Iraq and Afghanistan have higher rates of new-onset asthma than those who did not deploy. However, it is unknown whether combat experiences, in addition to deployment, contribute to new-onset asthma risk. This study aimed to longitudinally determine the risk factors for developing asthma, including combat deployment (categorized as deployed with combat experience, deployed without combat experience, or nondeployed), among participants in the Millennium Cohort Study from 2001 to 2013. A total of 75,770 participants completed a baseline survey and at least 1 triennial follow-up survey on deployment experiences, lifestyle characteristics, and health outcomes. Complementary log-log models stratified by sex were used to estimate the relative risk of developing asthma among participants who reported no history of asthma at baseline. In models with adjustments, those who deployed with combat experience were 24%–30% more likely to develop asthma than those who did not deploy. Deployed personnel without combat experience were not at a higher risk for new-onset asthma compared with nondeployers. Further research is needed to identify specific features of combat that are associated with greater asthma risk to inform prevention strategies.

asthma; combat disorders; longitudinal studies; military personnel; occupational exposure; respiratory system; veterans

Abbreviations: BMI, body mass index; CTS, Contingency Tracking System; OEF, Operation Enduring Freedom; OIF, Operation Iraqi Freedom; PTSD, posttraumatic stress disorder.

Over 2 million US service members have deployed in support of Operation Enduring Freedom (OEF), Operation Iraqi Freedom (OIF), and Operation New Dawn (1). Self-reported respiratory illnesses accounted for a large proportion of non-combat-related diagnoses, second only to diarrhea, in troops deployed in support of OEF/OIF (2). Asthma can have a negative impact on combat readiness by reducing service members' ability to perform military duties. For example, symptoms may interfere with essential activities (such as wearing a protective mask), require medications and treatments that are limited in a combat environment, and contribute to absence due to the need for medical attention, including potential evacuation and redeployment (2–5).

OEF, OIF, and Operation New Dawn are not the only conflicts during which respiratory complaints were reported by service members. Respiratory conditions have been a topic of

interest among Gulf War veterans (6–13) and continue to be a relevant concern. Several studies have been conducted, with mixed results, to determine whether deployment in support of OEF/OIF was associated with new-onset asthma (3, 4, 13–23). Those who deployed in support of the recent conflicts in Iraq and Afghanistan were found to have a significantly higher risk of new-onset asthma than their stateside counterparts (4, 21). On the other hand, one study of military medical records reported that the incidence of asthma diagnosis decreased by 6.3 cases per 10,000 person-years from 2001 to 2013 in all branches of the military, regardless of deployment status (24). However, this study was limited to active-duty service members and may have missed asthma diagnoses among personnel in the Reserve and National Guard components, as well as veterans.

Prospective epidemiologic studies investigating the incidence of asthma among US service members and veterans of

the current conflicts in Iraq and Afghanistan are lacking. The Millennium Cohort Study is a longitudinal study, including participants from all branches of the US military who are active-duty and Reserve/National Guard personnel. The survey includes a wide range of outcomes, exposures, and covariates that other studies have not been able to account for. Leveraging this large longitudinal population study, the present study investigated the relationship between combat deployment in support of OEF/OIF and new-onset asthma over a 12-year follow-up period.

METHODS

Study population and survey methods

The Millennium Cohort Study, the largest prospective cohort study in a military population, was launched in 2001 with the primary goal of evaluating the potential consequences that deployment and other military exposures may have on health (25, 26). Of the invited sample, the initial panel (Panel 1) enrolled 77,047 (35.9%) participants, who were randomly chosen from active US military rosters in October 2000, with oversampling of Reserve and National Guard personnel, women, and those who had been recently deployed. The second accession, Panel 2, enrolled 31,110 (25.3%) participants, who were randomly selected military personnel with 1–2 years of service as of October 2003. Panel 3, the third accession, enrolled 43,440 (28.2%) participants, who were randomly selected military personnel with 1–3 years of service as of October 2006. Panels 2 and 3 were oversampled for women and Marines. The Millennium Cohort Study survey consists of questions on lifestyle characteristics, military experiences, and health outcomes and behaviors. In addition to the baseline survey, participants are asked to complete a follow-up survey approximately every 3 years. Additional participant data were provided by the Defense Manpower Data Center, including sex, birth date, race/ethnicity, deployment in support of the recent operations in Iraq and Afghanistan, pay grade, service component, service branch, primary and duty occupations, date of separation from military service, and previous deployment experience to Southwest Asia, Bosnia, or Kosovo between 1998 and 2001 (27). A more detailed description of the study's sampling and methodology has been described elsewhere (25, 26). All participants provided informed consent, and the study was approved by the Naval Health Research Center Institutional Review Board.

Study design

Our study included Millennium Cohort Study participants from Panels 1, 2, and 3, from 2001 to 2013, who completed the baseline survey and at least the first triennial follow-up survey, and who were not missing covariate, exposure, or outcome data. Participants who reported a prior diagnosis of asthma on the baseline survey were excluded from the study population. Participants remained in the study until their final survey, defined as the survey at which new-onset asthma was reported or the last survey completed—whichever came first. Fixed covariates were measured at baseline, and time-varying covariates were measured at the survey prior to the final survey. The main exposure, combat deployment, was measured over the entire

follow-up period (from earliest available data until the follow-up survey prior to the final survey).

The outcome of interest, new-onset asthma, was obtained from the Millennium Cohort Study survey. At baseline, asthma was assessed with the following yes/no question, with asthma listed as one of several health conditions: "Has your doctor or other health professional ever told you that you have any of the following conditions?" At triennial follow-up, a similar question was asked, but the time frame was restricted to "the last 3 years" as opposed to "ever." New-onset asthma was defined by participants not reporting being diagnosed with asthma at baseline and then reporting being diagnosed with asthma in a subsequent survey.

The exposure of interest was combat deployment in support of OEF/OIF during the entire follow-up period, categorized as nondeployed, deployed without combat, and deployed with combat. Combat deployment was assessed using a combination of combat experiences endorsed on the Millennium Cohort Study survey, and deployment dates were obtained from the Contingency Tracking System (CTS) database maintained by the Defense Manpower Data Center. Combat experience was determined by asking participants whether they were personally exposed to any of the following combat items (excluding television, video, movies, computers, or theater): witnessing death, witnessing physical abuse, dead and/or decomposing bodies, maimed soldiers or civilians, or prisoners of war or refugees. The CTS provided in- and out-of-theater dates in support of OEF/OIF since 2001. Deployments in support of OEF/OIF included deployments to Iraq and Afghanistan as well as non-combat zones (e.g., Japan and Germany) and sea locations (e.g., Persian Gulf). A deployment based on the CTS in conjunction with endorsement of experiencing combat was defined as "deployed with combat." A deployment reported in the CTS in the absence of endorsement of any of the combat items was categorized as "deployed without combat." Participants who did not deploy during the study period, according to CTS data, were categorized as "nondeployed." Combat deployment was assessed at baseline and each follow-up prior to the final survey (follow-up period). Once a participant was categorized as deployed with combat, this status was retained for the entire follow-up period. Similarly, in the absence of being deployed with combat, being deployed without combat was carried forward. This carry-forward method was used to ensure that the association between exposure and new-onset asthma could be measured without restricting the exposure to only the 3 years prior to new-onset asthma.

Additional covariates included demographic factors, military characteristics, smoking status, environmental exposures, enrollment panel, number of life stressor events, and posttraumatic stress disorder (PTSD) status. Demographic characteristics included birth year, sex, race/ethnicity, marital status, and education. Body mass index (BMI) was calculated as self-reported weight in kilograms divided by height in meters, squared (kg/m^2). Service branch, service component, military occupation, military service status, and prior deployment completed the set of military characteristics. Smoking status was classified as nonsmoker, former smoker, or current smoker. Current smokers were those who reported smoking at least 100 cigarettes (5 packs) in their lifetime and had not quit successfully, while former smokers were those who reported

smoking at least 100 cigarettes in their lifetime and successfully quit. Nonsmokers were those who answered “no” to smoking at least 100 cigarettes in their lifetime. Environmental exposures were ascertained from report of being personally exposed to: 1) occupational hazards requiring protective equipment, such as respirators or hearing protection; 2) routine skin contact with paint, solvent, and/or substances; 3) pesticides, including creams, sprays, or uniform treatments; and 4) pesticides applied in the environment or around living facilities in the last 3 years. Potential responses were “yes,” “no,” or “don’t know.” As a result of high collinearity, the pesticide questions (items 3 and 4) were combined into one variable. If a participant answered “yes” to either item, then “yes” was retained for the combined variable. If either item was answered as “don’t know,” the combined variable retained the “don’t know” response. Otherwise, the combined variable was set as “no.” Life stress events were assessed at baseline as ever experienced and at follow-up as experienced in the last 3 years. Life stress was categorized as no event, 1 event, or more than 1 event from the following list: divorce or separation, financial problems, sexual assault, sexual harassment, physical assault, or suffered a disabling illness or injury. PTSD status was based on the PTSD Checklist–Civilian Version, using the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*, sensitive diagnostic criteria. In an analysis of Millennium Cohort Study data, the PTSD Checklist–Civilian Version had high internal consistency (Cronbach’s $\alpha = 0.94$) (28). All covariates were assessed at baseline; BMI, military service status, smoking status, environmental exposures, number of stressful life events, and PTSD status were also updated at each available follow-up prior to the final survey.

Additional deployment characteristics were assessed for those participants who had been deployed during the follow-up period. Multiple deployments was defined as having more than 1 deployment during the entire follow-up period, and duration of deployment was defined as the cumulative number of days deployed during the entire follow-up period.

Statistical analysis

Bivariate analyses, including χ^2 tests of association, were performed to investigate the relationship between new-onset asthma and combat deployment as well as occupational, demographic, and behavioral risk factors. Analyses were stratified by sex because women are known to have a higher prevalence of adult asthma compared with men (29). Because new-onset asthma was reported at the time of follow-up survey administration rather than at the time of diagnosis, discrete-time survival analysis was used to investigate the association of combat deployment with new-onset asthma that occurred during each follow-up time interval. The analysis assumes an underlying continuous-time proportional hazards model, and a complementary log-log model was fitted. Time at risk was calculated from study entry (baseline survey completion) until the outcome was measured or the last completed survey—whichever came first. Relative risks were estimated, and 95% confidence intervals were reported.

Collinearity was assessed using the variance inflation factor, where a value >4 indicates possible collinearity. All covariates remained in the model, regardless of significance, to facilitate

comparisons between results among men and women. All 3 panels were pooled for these analyses. Additional analyses, restricted to those who deployed during the follow-up period, assessed whether new-onset asthma was associated with multiple deployments or the cumulative number of days deployed. Data management and statistical analyses were performed using SAS, version 9.3 (SAS Institute, Inc., Cary, North Carolina).

RESULTS

The eligible study population consisted of participants who submitted at least a baseline and first follow-up survey ($n = 94,241$) and screened negative for lifetime asthma diagnosis at baseline ($n = 87,914$). Participants whose surveys were missing asthma status at first follow-up ($n = 2,668$), had undetermined combat deployment status at baseline ($n = 241$), or had missing covariate data ($n = 9,235$) were excluded, resulting in a final study population of 75,770 participants.

Population characteristics are shown in Table 1. During follow-up, 1,452 (2.7%) men and 1,055 (4.6%) women developed asthma, and those who were not deployed had the highest proportion of new-onset asthma (3.1% and 5.0%, respectively), followed by those who deployed with combat experience (2.7% and 4.4%, respectively) and those who deployed without combat experience (1.6% and 3.0%, respectively). Women consistently had higher rates of new-onset asthma than did men for all categories of characteristics listed in Table 1. Among both men and women, older participants, those who were divorced/widowed/separated, those with a higher BMI, those in the Army, those of enlisted rank, those with more than 1 stressful life event, those with PTSD, and those who did not know whether they had been personally exposed to occupational hazards requiring protective equipment had higher rates of new-onset asthma. Results also indicated higher incidence of new-onset asthma among those who self-reported routine skin contact with paints/solvents/substances and pesticides, including creams, sprays, and uniform treatments, and exposure to pesticides applied in the environment/surroundings (Table 1).

Men and women who deployed with combat experience during the follow-up period had a higher risk of new-onset asthma compared with those who did not deploy, after adjusting for covariates (for men, relative risk = 1.30, 95% confidence interval: 1.14, 1.47; for women, relative risk = 1.24, 95% confidence interval: 1.05, 1.46) (Table 1). Among both men and women, Hispanic ethnicity, being overweight or obese, Army service, experiencing more than 1 stressful life event, PTSD, and health care or other technical and specialty (e.g., mapping, weather, ordnance disposal, or diving) occupations were risk factors for new-onset asthma in mutually adjusting models. Among men, additional risk factors included active-duty status, enlisted rank, experiencing 1 stressful life event, and occupations in functional support and service and supply. Additional risk factors among women included Asian/Pacific Islander race/ethnicity, being divorced/widowed/separated, separation from military service, non-occupations (e.g., patients, prisoners, and students) and communications/intelligence occupations, and answering “yes” to being personally exposed to pesticides, including creams, sprays, and uniform treatments, and pesticides applied in the environment/surroundings.

Table 1. Descriptive Characteristics of the Study Population, Incidence of New-Onset Asthma, and Adjusted Relative Risk of Self-Reported New-Onset Asthma According to Sex, Millennium Cohort Study, United States, 2001–2013

Characteristic	Men ^{a,b} (n = 52,826)				Women ^{a,c} (n = 22,944)			
	No.	New-Onset Asthma, %	RR	95% CI	No.	New-Onset Asthma, %	RR	95% CI
Exposure of interest								
Combat deployment during follow-up ^d								
Not deployed	29,237	3.1	1.00	Referent	15,678	5.0	1.00	Referent
Deployed without combat experience	8,922	1.6	0.97	0.83, 1.15	3,577	3.0	0.97	0.80, 1.18
Deployed with combat experience	14,667	2.7	1.30	1.14, 1.47	3,689	4.4	1.24	1.05, 1.46
Demographic factors								
Race/ethnicity								
White, non-Hispanic	41,880	2.7	1.00	Referent	15,895	4.4	1.00	Referent
Black, non-Hispanic	4,484	3.1	1.01	0.85, 1.20	3,692	5.1	1.06	0.90, 1.24
Asian/Pacific Islander	1,899	2.1	0.91	0.67, 1.22	1,051	4.6	1.44	1.12, 1.86
Hispanic	3,414	3.7	1.28	1.08, 1.53	1,701	5.5	1.37	1.13, 1.66
Other	1,149	2.5	0.84	0.59, 1.20	605	5.1	1.15	0.82, 1.61
Birth year								
1980 or later	14,454	2.0	1.00	Referent	9,435	3.4	1.00	Referent
1970–1979	15,078	2.8	0.94	0.78, 1.14	6,754	5.0	1.14	0.96, 1.36
Before 1970	23,294	3.2	0.96	0.77, 1.21	6,755	5.9	1.19	0.96, 1.48
Marital status								
Never married	14,362	2.1	0.88	0.77, 1.01	9,257	4.4	1.13	0.99, 1.30
Married	34,164	3.0	1.00	Referent	9,841	4.3	1.00	Referent
Divorced/widowed/separated	4,300	3.2	0.89	0.75, 1.05	3,846	6.0	1.19	1.02, 1.38
Education								
High school degree/GED or less	9,686	2.5	0.95	0.79, 1.15	3,296	4.1	0.9	0.71, 1.14
Some college or associate degree	26,452	3.0	1.02	0.88, 1.19	12,142	4.9	1.13	0.95, 1.34
Bachelor degree or higher	16,688	2.5	1.00	Referent	7,506	4.3	1.00	Referent
BMI ^{e,f}								
Underweight/normal (<25.0)	14,872	2.2	1.00	Referent	13,182	4.1	1.00	Referent
Overweight (25.0–29.9)	28,516	2.8	1.30	1.14, 1.47	7,498	5.2	1.36	1.20, 1.53
Obese (≥30.0)	9,438	3.4	1.88	1.62, 2.18	2,264	5.6	1.68	1.42, 2.00
Enrollment panel ^g								
2001–2003	32,852	3.2	1.00	Referent	10,878	5.8	1.00	Referent
2004–2006	8,016	2.6	0.97	0.81, 1.16	5,024	4.3	1.01	0.85, 1.20
2007–2008	11,958	1.7	0.74	0.59, 0.92	7,042	2.9	0.76	0.62, 0.95
Military service								
Service branch								
Army	23,206	3.5	1.00	Referent	10,464	5.5	1.00	Referent
Navy/Coast Guard	9,354	2.4	0.79	0.69, 0.91	4,309	4.4	0.96	0.82, 1.12
Marine Corps	4,877	2.0	0.68	0.55, 0.84	676	4.4	0.98	0.70, 1.39
Air Force	15,389	2.1	0.69	0.61, 0.79	7,495	3.5	0.79	0.69, 0.91
Service component								
Active duty	32,986	2.7	1.00	Referent	13,354	4.5	1.00	Referent
Reserve/Guard	19,840	2.8	0.83	0.74, 0.93	9,590	4.8	0.93	0.82, 1.05

Table continues

Table 1. Continued

Characteristic	Men ^{a,b} (n = 52,826)				Women ^{a,c} (n = 22,944)			
	No.	New-Onset Asthma, %	RR	95% CI	No.	New-Onset Asthma, %	RR	95% CI
Occupation								
Infantry, gun crews, seamen (combat specialist)	12,285	2.5	1.00	Referent	1,429	3.4	1.00	Referent
Electrical repair	5,703	2.4	1.11	0.92, 1.34	1,512	3.3	0.93	0.65, 1.33
Communication/intelligence	4,263	3.1	1.17	0.96, 1.43	1,951	5.4	1.56	1.14, 2.15
Health care	3,745	3.2	1.26	1.03, 1.55	5,002	4.8	1.41	1.05, 1.88
Other technical and specialty	1,475	3.3	1.54	1.18, 2.03	698	4.7	1.51	1.01, 2.25
Functional support	7,403	3.1	1.34	1.14, 1.58	6,664	4.7	1.21	0.91, 1.62
Electrical/mechanical equipment repair	9,041	2.7	1.17	0.99, 1.38	1,734	3.8	1.00	0.70, 1.42
Craft workers	1,878	2.7	1.26	0.96, 1.65	422	4.0	0.97	0.58, 1.62
Service and supply	4,503	3.2	1.30	1.08, 1.57	2,318	5.7	1.32	0.96, 1.81
Non-occupation	2,530	1.7	0.85	0.63, 1.16	1,214	4.5	1.63	1.14, 2.32
Pay grade								
Enlisted	40,620	2.9	1.25	1.05, 1.49	17,984	4.8	1.14	0.93, 1.39
Officer ^h	12,206	2.3	1.00	Referent	4,960	4.0	1.00	Referent
Military service status ^f								
Currently serving	44,404	2.9	1.00	Referent	19,450	4.6	1.00	Referent
Former service member	8,422	1.9	1.00	0.87, 1.16	3,494	4.4	1.37	1.17, 1.59
Prior deployment ⁱ								
Yes	12,082	3.0	0.96	0.84, 1.09	1,429	5.6	0.98	0.79, 1.21
No	40,744	2.7	1.00	Referent	21,515	4.5	1.00	Referent
Behavioral factors								
Smoking status ^f								
Nonsmoker	30,367	2.7	1.00	Referent	14,553	4.3	1.00	Referent
Former smoker	13,540	2.8	0.93	0.83, 1.05	5,163	5.0	1.11	0.97, 1.27
Current smoker	8,919	2.9	1.01	0.88, 1.16	3,228	5.3	1.09	0.92, 1.28
Environmental exposures								
Occupational hazards requiring protective equipment ^f								
Yes	27,680	3.0	0.97	0.86, 1.09	7,358	5.4	1.13	0.99, 1.29
No	24,104	2.5	1.00	Referent	15,139	4.2	1.00	Referent
Don't know	1,042	3.4	1.09	0.80, 1.50	447	5.6	1.11	0.76, 1.63
Routine skin contact with paints/solvents/substances ^f								
Yes	13,011	3.4	1.11	0.98, 1.26	2,881	5.7	1.00	0.84, 1.19
No	37,463	2.5	1.00	Referent	19,271	4.4	1.00	Referent
Don't know	2,352	3.7	1.17	0.93, 1.47	792	5.1	0.93	0.68, 1.27
Pesticides, including creams, sprays, and uniform treatments, and applied in the environment/surroundings ^f								
Yes	19,133	3.2	1.08	0.96, 1.21	6,238	5.7	1.18	1.03, 1.35
No	29,579	2.4	1.00	Referent	14,732	4.1	1.00	Referent
Don't know	4,114	3.2	1.01	0.84, 1.21	1,974	5.0	0.99	0.80, 1.21
Stressors								
Life stressor events ^{f,j}								
None	40,568	2.2	1.00	Referent	14,243	3.5	1.00	Referent
1 event	9,401	4.2	1.31	1.16, 1.47	5,231	5.4	1.11	0.97, 1.27
>1 event	2,857	5.6	1.37	1.15, 1.62	3,470	8.0	1.31	1.12, 1.52

Table continues

Table 1. Continued

Characteristic	Men ^{a,b} (n = 52,826)				Women ^{a,c} (n = 22,944)			
	No.	New-Onset Asthma, %	RR	95% CI	No.	New-Onset Asthma, %	RR	95% CI
PTSD ^{f,k}								
Yes	2,840	4.8	1.82	1.55, 2.15	1,506	7.8	1.56	1.30, 1.88
No	49,986	2.6	1.00	Referent	21,438	4.4	1.00	Referent

Abbreviations: BMI, body mass index; CI, confidence interval; GED, General Educational Development certificate; PTSD, posttraumatic stress disorder; RR, relative risk.

^a Univariate analyses were performed separately for men and women. For both sexes, combat deployment, birth year, marital status, education, BMI, enrollment panel, service branch, occupation, pay grade, environmental exposures, life stressor events, and PTSD were significantly associated with new-onset asthma ($\alpha = 0.05$). Models were fitted separately for men and women; both models adjusted for all variables in the table.

^b Among men, race/ethnicity and military service status were also significantly associated with new-onset asthma ($\alpha = 0.05$).

^c Among women, smoking status was also significantly associated with new-onset asthma ($\alpha = 0.05$).

^d Deployment was defined as being deployed in support of Operation Enduring Freedom or Operation Iraqi Freedom. Combat was defined as reporting personal exposure to ≥ 1 of the following: witnessing death, witnessing physical abuse, dead and/or decomposing bodies, maimed soldiers or civilians, or prisoners of war or refugees. Combat deployment was assessed over the entire follow-up period.

^e BMI was calculated as weight (kg) divided by height (m) squared.

^f Time-varying covariates were measured at the survey prior to the final survey (the survey at which new-onset asthma was reported or the last survey completed, whichever came first).

^g This study used 3 panels of Millennium Cohort Study participants. Participants completed their baseline survey during the listed years (Panel 1: 2001–2003, Panel 2: 2004–2006, Panel 3: 2007–2008).

^h Officer includes commissioned and warrant officers.

ⁱ Prior deployments to Bosnia, Kosovo, or Southwest Asia between January 1, 1998, and September 1, 2001.

^j Categorized number of endorsements of the following events: divorce or separation, financial problems, sexual assault, sexual harassment, physical assault, or suffered a disabling illness or injury.

^k Based on the PTSD Checklist–Civilian Version, using sensitive diagnostic criteria from the *Diagnostic and Statistical Manual of Mental Disorder, Fourth Edition*.

Among the 31,152 participants who deployed, 23,797 (76.4%) were men and 7,355 (23.6%) were women (Table 2). Among this group, 547 (2.3%) men and 272 (3.7%) women developed asthma during the follow-up period. No significant association was found between multiple deployments and new-onset asthma (Table 2). A significant association was found between deployment duration and new-onset asthma, after adjusting for covariates; however, deployment duration was not independently significantly associated with new-onset asthma. No collinearity was observed between the independent variables included in the models shown in Tables 1 and 2.

DISCUSSION

Our study results indicate that combat deployment was associated with a 24%–30% higher risk of new-onset asthma, after adjusting for demographic and military characteristics, smoking status, environmental exposures, number of life stressor events, and PTSD status. This finding suggests an elevated risk of asthma in a population of deployed military personnel who are considered to be healthier than those who did not deploy (healthy deployer effect). In addition to combat deployment, other demographic and military characteristics, environmental exposures, and stressors were associated with new-onset asthma.

Demographic characteristics significantly associated with asthma included race/ethnicity, marital status, and BMI. We

observed that Hispanic men and women were 28%–37% more likely to develop asthma than non-Hispanic white personnel. We also observed, among women in our sample, that Asian/Pacific Islander women were 44% more likely to report new-onset asthma than non-Hispanic white women. This finding is inconsistent with reports of lower prevalence of asthma among Asian Americans, especially among those born outside the United States (30). However, this lower prevalence among Asian Americans may be driven by nativity, given that foreign-born Asian Americans would be less likely to enter the military than those born in the United States (31). Consistent with other clinical, epidemiologic, and systematic studies evaluating body size and asthma, the risk for new-onset asthma was associated with increasing BMI in our analysis (32–36). In our study, the highest risk for asthma among men and women, when adjusted for all covariates, was among those having a BMI of 30 or above (68%–88% higher risk).

Military characteristics significantly associated with asthma included service branch, service component, occupation, pay grade, and military service status. Differences in exposure among men deployed to ground operations may explain the observed differences in risk of new-onset asthma by service branch, service component, and pay grade. Among men, Army service conferred the highest risk of new-onset asthma among the service branches; enlisted personnel had a 25% higher risk compared with officers, and Reserve/National Guard had a 17% lower risk compared with their active-duty counterparts. Certain occupations, including health care, have been associated

Table 2. Multiple Deployments, Deployment Duration, and Adjusted Relative Risk of New-Onset Asthma According to Sex Among Deployed Personnel (*n* = 31,152), Millennium Cohort Study, United States, 2001–2013

Characteristics	Men ^a (<i>n</i> = 23,797)				Women ^a (<i>n</i> = 7,355)			
	No.	New-Onset Asthma, %	RR	95% CI	No.	New-Onset Asthma, %	RR	95% CI
Multiple deployments ^{b,c}								
Yes	6,452	2.1	0.99	0.82, 1.20	1,442	3.3	0.95	0.70, 1.28
No	17,345	2.4	1.00	Referent	5,913	3.8	1.00	Referent
Deployment duration ^{b,d}								
1–200 days	10,231	2.1	1.00	Referent	3,555	3.4	1.00	Referent
201–400 days	9,521	2.4	1.08	0.88, 1.32	2,979	4.3	1.16	0.89, 1.53
401–600 days	2,683	2.8	1.35	1.02, 1.78	575	2.3	0.71	0.41, 1.22
>600 days	1,362	1.8	0.91	0.59, 1.37	246	4.5	1.54	0.85, 2.80

Abbreviations: CI, confidence interval; PTSD, posttraumatic stress disorder; RR, relative risk.

^a Models were fitted separately for men and women. Both models mutually adjusted for race/ethnicity, birth year, marital status, education, body mass index, panel, service branch, service component, occupation, pay grade, separation from the military, and prior deployment to Bosnia, Kosovo, or Southwest Asia between January 1, 1998, and September 1, 2001; smoking status, occupational hazards requiring protective equipment, routine skin contact with paints/solvents/substances, and exposure to pesticides, including creams, sprays, and uniform treatments, and pesticides applied in the environment/surroundings; life stressor events; and PTSD.

^b Separate models were fitted for multiple deployments and deployment duration.

^c Multiple deployments were defined as deploying in support of Operation Iraqi Freedom or Operation Enduring Freedom more than once during the follow-up period.

^d Deployment duration was defined as the cumulative number of days deployed in support of Operation Iraqi Freedom or Operation Enduring Freedom during the follow-up period.

with a higher risk of new-onset asthma in nonmilitary populations (37). Compared with combat specialists, health care was significantly associated with asthma in our study.

Among women, new-onset asthma was associated with self-reported exposure to pesticides, but, due to the broad wording of the survey question, we were unable to distinguish whether this was attributable to specific uses, chemical classes, or application methods. In numerous Periodic Occupational and Environmental Monitoring Summary reports of environmental hazards at operating bases in theater, permethrin and other insecticides, rodenticides, and herbicides were used for pest control at bases (38). While not available for study participants in this analysis, in-country region of deployment or base location could serve as a proxy for environmental exposures. Several studies have investigated the association between pesticides and adult asthma but have reported inconsistent findings (39).

Although smoking has been associated with exacerbation of asthma symptoms, a recent review indicated there was insufficient evidence to infer a causal relationship with new-onset asthma (40). We observed no significant association between asthma and smoking status in our study population.

Prolonged exposure to stress may trigger or exacerbate the symptoms of asthma (41). Allostatic load (the wearing down of the body following repeated stress) (42) has been found to be associated with higher asthma risk (43) and may explain the observed association between combat deployment and new-onset asthma. Our results also suggest a possible dose-dependent increase in asthma risk among those experiencing more than 1 stressful life event compared with those who

experienced only 1 stressful life event. The observed associations between new-onset asthma and PTSD and stressful life events may also be manifestations of allostatic load.

One of the limitations of this analysis is that the findings may be susceptible to recall and reporting bias due to our reliance on self-reported survey data. However, the survey instruments employed were validated and consistently administered over follow-up surveys (28). In addition, Oksanen et al. (44) observed high validity of self-reported physician diagnoses of incident asthma (63% sensitivity and 91% specificity) and prevalent asthma (91% sensitivity and 97% specificity) when compared with health records. Electronic military medical records were not used because this information is available only for active-duty and activated Reserve or National Guard personnel; these data are not available for separated personnel and inactivated Reserve or National Guard personnel. However, we did compare self-reported asthma endorsements with medical record diagnoses among 4,477 eligible individuals. We found 50.4 positive agreement and 97.6 negative agreement, consistent with a prior Millennium Cohort analysis for acute conditions that included asthma and a Finnish public-sector employee study (45). The measurement of stressful life events is limited in the Millennium Cohort Study because the items focus on several general categories and do not measure all types of stressors or the subjective experience of stress. Because self-reported asthma diagnosis was based on the 3 years preceding completion of the follow-up survey, the exact timing of asthma development and combat exposure could not be determined. Furthermore, the 5-item combat questions were not necessarily specific to a particular deployment. However,

the longitudinal nature of this study did eliminate many of the limitations that previous cross-sectional studies have encountered and allowed for investigation of the temporal associations between combat deployment and asthma.

Despite these limitations, the large sample size and population-based design with up to 12 years of prospective follow-up allowed us to identify incident asthma cases among participants from all branches of the military, including active-duty and Reserve/National Guard personnel and those who separated from military service. This design also allowed us to exclude prevalent cases of asthma at baseline. In addition, important covariates, such as smoking and BMI, were also available in these prospective data.

To our knowledge, this is the only longitudinal, prospective epidemiologic study that has examined the association between combat deployment and new-onset asthma with over a decade of follow-up. These findings indicate a higher risk of new-onset asthma among those who deployed and experienced combat compared with those who did not deploy, but there was no observed change in risk among those who deployed without combat experience compared with those who did not deploy. This implies that specific attributes of combat or other deployment exposures and experiences may drive the association with elevated risk of new-onset asthma. Further research is needed to identify specific aspects of combat deployment that are associated with greater asthma risk, the knowledge of which can form the basis for prevention strategies among military service members.

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REFERENCES

1. Committee on the Assessment of the Readjustment Needs of Military Personnel, Veterans, and Their Families; Board on the Health of Select Populations; Institute of Medicine. *Returning Home from Iraq and Afghanistan: Assessment of Readjustment Needs of Veterans, Service Members, and Their Families*. Washington, DC: The National Academies Press; 2014.
2. Sanders JW, Putnam SD, Frankart C, et al. Impact of illness and non-combat injury during Operations Iraqi Freedom and Enduring Freedom (Afghanistan). *Am J Trop Med Hyg*. 2005; 73(4):713–719.
3. Roop SA, Niven AS, Calvin BE, et al. The prevalence and impact of respiratory symptoms in asthmatics and nonasthmatics during deployment. *Mil Med*. 2007;172(12):1264–1269.
4. Szema AM, Peters MC, Weissinger KM, et al. New-onset asthma among soldiers serving in Iraq and Afghanistan. *Allergy Asthma Proc*. 2010;31(5):67–71.

5. Sessions CK. Asthma, active component, US Armed forces, 1999–2008. *MSMR*. 2009;16(7):5.
6. Karlinsky JB, Blanchard M, Alpern R, et al. Late prevalence of respiratory symptoms and pulmonary function abnormalities in Gulf War I Veterans. *Arch Intern Med*. 2004;164(22):2488–2491.
7. Gray GC, Callahan JD, Hawksworth AW, et al. Respiratory diseases among US military personnel: countering emerging threats. *Emerg Infect Dis*. 1999;5(3):379–385.
8. Gray GC, Kaiser KS, Hawksworth AW, et al. Increased postwar symptoms and psychological morbidity among US Navy Gulf War veterans. *Am J Trop Med Hyg*. 1999;60(5):758–766.
9. Richards AL, Hyams KC, Watts DM, et al. Respiratory disease among military personnel in Saudi Arabia during Operation Desert Shield. *Am J Public Health*. 1993;83(9):1326–1329.
10. Young RC, Jr, Rachal RE, Huguley JW, 3rd. Environmental health concerns of the Persian Gulf War. *J Natl Med Assoc*. 1992;84(5):417–424.
11. Coker WJ, Bhatt BM, Blatchley NF, et al. Clinical findings for the first 1000 Gulf war veterans in the Ministry of Defence's medical assessment programme. *BMJ*. 1999;318(7179):290–294.
12. Iowa Persian Gulf Study Group. Self-reported illness and health status among Gulf War veterans: a population-based study. The Iowa Persian Gulf Study Group. *JAMA*. 1997;277(3):238–245.
13. Weese CB, Abraham JH. Potential health implications associated with particulate matter exposure in deployed settings in Southwest Asia. *Inhal Toxicol*. 2009;21(4):291–296.
14. Abraham JH, DeBakey SF, Reid L, et al. Does deployment to Iraq and Afghanistan affect respiratory health of US military personnel? *J Occup Environ Med*. 2012;54(6):740–745.
15. Baird CP, DeBakey S, Reid L, et al. Respiratory health status of US Army personnel potentially exposed to smoke from 2003 Al-Mishraq Sulfur Plant fire. *J Occup Environ Med*. 2012;54(6):717–723.
16. Morris MJ, Zacher LL, Jackson DA. Investigating the respiratory health of deployed military personnel. *Mil Med*. 2011;176(10):1157–1161.
17. Rose CS. Military service and lung disease. *Clin Chest Med*. 2012;33(4):705–714.
18. Smith B, Wong CA, Boyko EJ, et al. The effects of exposure to documented open-air burn pits on respiratory health among deployers of the Millennium Cohort Study. *J Occup Environ Med*. 2012;54(6):708–716.
19. Smith B, Wong CA, Smith TC, et al. Newly reported respiratory symptoms and conditions among military personnel deployed to Iraq and Afghanistan: a prospective population-based study. *Am J Epidemiol*. 2009;170(11):1433–1442.
20. DelVecchio SP, Collen JF, Zacher LL, et al. The impact of combat deployment on asthma diagnosis and severity. *J Asthma*. 2015;52(4):363–369.
21. Abraham JH, Eick-Cost A, Clark LL, et al. A retrospective cohort study of military deployment and postdeployment medical encounters for respiratory conditions. *Mil Med*. 2014;179(5):540–546.
22. Barth SK, Dursa EK, Peterson MR, et al. Prevalence of respiratory diseases among veterans of Operation Enduring Freedom and Operation Iraqi Freedom: results from the National Health Study for a New Generation of US Veterans. *Mil Med*. 2014;179(3):241–245.
23. Piccirillo AL, Packnett ER, Cowan DN, et al. Epidemiology of asthma-related disability in the US Armed Forces: 2007–2012. *J Asthma*. 2016;53(7):668–678.
24. Abraham JH, Clark LL, Sharkey JM, et al. Trends in rates of chronic obstructive respiratory conditions among US military personnel, 2001–2013. *US Army Med Dep J*. 2014;33–43.
25. Gray GC, Chesbrough KB, Ryan MA, et al. The Millennium Cohort Study: a 21-year prospective cohort study of 140,000 military personnel. *Mil Med*. 2002;167(6):483–488.
26. Ryan MA, Smith TC, Smith B, et al. Millennium Cohort: enrollment begins a 21-year contribution to understanding the impact of military service. *J Clin Epidemiol*. 2007;60(2):181–191.
27. Defense Manpower Data Center, US Department of Defense. Personnel data. https://www.dmdc.osd.mil/appj/dwp/personnel_data.jsp. Accessed October 01, 2016.
28. Smith TC, Smith B, Jacobson IG, et al. Reliability of standard health assessment instruments in a large, population-based cohort study. *Ann Epidemiol*. 2007;17(7):525–532.
29. Akinbami LJ, Moorman JE, Bailey C, et al. Trends in asthma prevalence, health care use, and mortality in the united states, 2001–2010. *NCHS Data Brief*. 2012;(94):1–8.
30. Bhan N, Kawachi I, Glymour MM, et al. Time Trends in Racial and Ethnic Disparities in Asthma Prevalence in the United States From the Behavioral Risk Factor Surveillance System (BRFSS) Study (1999–2011). *Am J Public Health*. 2015;105(6):1269–1275.
31. Batalova J. Immigrants in the US Armed Forces. <https://www.migrationpolicy.org/article/immigrants-us-armed-forces>. Published May 15, 2008. Accessed October 18, 2016.
32. Barros R, Moreira P, Padrão P, et al. Obesity increases the prevalence and the incidence of asthma and worsens asthma severity. *Clin Nutr*. 2017;36(4):1068–1074.
33. Boulet LP. Asthma and obesity. *Clin Exp Allergy*. 2013;43(1):8–21.
34. Leinaar E, Alamian A, Wang L. A systematic review of the relationship between asthma, overweight, and the effects of physical activity in youth. *Ann Epidemiol*. 2016;26(7):504–510.e6.
35. Çelebi Sözen Z, Aydın Ö, Mungan D, et al. Obesity-asthma phenotype: effect of weight gain on asthma control in adults. *Allergy Asthma Proc*. 2016;37(4):311–317.
36. Urban N, Boivin MR, Cowan DN. Fitness, obesity and risk of asthma among Army trainees. *Occup Med (Lond)*. 2016;66(7):551–557.
37. Kim JL, Torén K, Lohman S, et al. Respiratory symptoms and respiratory-related absence from work among health care workers in Sweden. *J Asthma*. 2013;50(2):174–179.
38. US Army Public Health Center. Periodic Occupational and Environmental Monitoring Summary (POEMS). <https://phc.amedd.army.mil/topics/envirohealth/hrasm/Pages/POEMS.aspx>. Accessed May 1, 2017.
39. Prince Edward Island Canada Health and Wellness. *Pesticides and Human Health. Part 2: PEI Health and Pesticide Use*. Prince Edward Island, Canada: Prince Edward Island Canada Health and Wellness; 2015.
40. Warren GW, Alberg AJ, Kraft AS, et al. The 2014 Surgeon General's report: "The health consequences of smoking—50 years of progress": a paradigm shift in cancer care. *Cancer*. 2014;120(13):1914–1916.
41. Rod NH, Kristensen TS, Lange P, et al. Perceived stress and risk of adult-onset asthma and other atopic disorders: a longitudinal cohort study. *Allergy*. 2012;67(11):1408–1414.
42. Juster RP, McEwen BS, Lupien SJ. Allostatic load biomarkers of chronic stress and impact on health and cognition. *Neurosci Biobehav Rev*. 2010;35(1):2–16.
43. Bahreinian S, Ball GD, Vander Leek TK, et al. Allostatic load biomarkers and asthma in adolescents. *Am J Respir Crit Care Med*. 2013;187(2):144–152.
44. Oksanen T, Kivimäki M, Pentti J, et al. Self-report as an indicator of incident disease. *Ann Epidemiol*. 2010;20(7):547–554.
45. Smith B, Chu LK, Smith TC, et al. Challenges of self-reported medical conditions and electronic medical records among members of a large military cohort. *BMC Med Res Methodol*. 2008;8:37.

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